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Client/Matter No.: CARP-0057; Serial No. 08/846,658

SENDER'S NAME: Doreen Y. Trujillo

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DOCKET NO.: CARP-0057

PATENT

RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP NO. 1642

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of: Adair et al.

Serial No.: 08/846,658

Group No.: 1642

Filed: May 1, 1997

Examiner: J. Burke

For: Humanised Antibodies

I, Doreen Yatko Trujillo, Registration No. 35,719 certify that this correspondence is being transmitted by facsimile to Examiner Burke of the U.S. Patent and Trademark Office, Washington, D.C. 20231.

On

Doreen Yatko Trujillo Reg. No. 35,719

BOX AF

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

REQUEST FOR RECONSIDERATION

This paper is being filed following the notice of appeal filed November 29, 1999, received by the Patent Office December 1, 1999. Applicants hereby petition for an extension of time of four-months and the undersigned authorizes the Examiner to charge the appropriate fee therefor to Deposit Account 23-3050.

Claims 24-31 were pending. In the Final Rejection, all pending claims were rejected. Amendments following the Final Rejection attempting to add claim 49 were not entered. In an effort to advance the case, claim 49 is not resubmitted herein. Applicants

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DOCKET NO.: CARP-0057**PATENT**

respectfully submit that allowable subject matter has been identified and request that the interference be declared.

Preliminarily, it is noted that the Examiner stated that the Information Disclosure Statements filed in the parent cases will be considered once the references are submitted. To the extent the Examiner is requiring that Applicants resubmit references already submitted, this appears to be contrary to MPEP § 609, page 600-103. Applicants are not required to resubmit references to get them considered by the Examiner.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 24-31 were again rejected in the Final Rejection under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection for the reasons that follow. For the Examiner's convenience, the paragraphs are designated to correspond to the Examiner's paragraphs for the rejection remaining under this section.

a. and b. The Examiner again rejected claims 24 and 28 alleging that the specification does not provide support for the concept that only substitutions adjacent CDRs are envisaged. Claims 24 and 28 were previously amended to recite that each of the donor amino acids to be replaced is adjacent a CDR or contributes to antigen binding as determined by X-ray crystallography. During a telephone conference between the Examiner and the undersigned, the Examiner indicated that removal of the "adjacent to a CDR" language would

DOCKET NO.: CARP-0057**PATENT**

obviate this rejection. Although Applicants disagree with the Examiner's reasoning, the claims have been amended herein to remove the recitation "adjacent to a CDR in the donor immunoglobulin sequence." As Applicants made clear in the previous response, the contribution to antigen binding need not be direct and, indeed, can be indirect, e.g., by affecting antigen binding site topology or inducing stable packing. Naturally, even for an indirect effect, the residues must be spatially near the CDR.

Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(e)

Claims 24-31 were again rejected under 35 U.S.C. § 102(e) in view of the Queen patent. Applicants respectfully traverse this rejection. Again, the relevant inquiry as to whether the Queen patent is an appropriate reference under 102(e) is whether there is support for the claims *as allowed* in the priority applications, see MPEP 2136.03, p. 2100-85, citing *In re Wertheim*, 209 USPQ 554 (CCPA 1981), not simply whether the limitations can be found in the priority document. Regardless, Applicants maintain that several of the limitations recited in the claims as allowed in the Queen patent do not find support in the two earliest Queen priority applications - i.e., Queen priority Application Serial No. 07/290,975, filed December 28, 1988 ("Queen '975") and Queen priority Application Serial No. 08/310,252, filed February 13, 1989 ("Queen '252"). For the Examiner's convenience, a chart delineating those limitations for which Applicants submit there is no support in Queen '975 and Queen '252 is attached as Appendix A. The Queen priority applications do not provide a written description of the invention as claimed in the Queen patent. 35 U.S.C. § 112, 1st ¶. The

DOCKET NO.: CARP-0057**PATENT**

claims as issued are not completely within the scope of the parent case generic disclosure. *In re Ahlbrecht*, 168 USPQ 293, 296 (CCPA 1971). Thus, the effective filing date of the Queen patent cannot be earlier than September 28, 1990, the next priority date. As evidenced by Appendix C, discussed *infra*, Applicants are entitled to their GB priority date of December 21, 1989. Accordingly, the Queen patent is not an appropriate reference under 35 U.S.C. § 102 (e), and this rejection should be withdrawn.

One of the limitations for which there is no support is the recitation "outside the Kabat and Chothia CDRs." This limitation is significant because the "CDRs" as defined by Kabat and Chothia differ.¹ Kabat defines CDR1 of the heavy chain as amino acids 31-35. Chothia defines the first hypervariable loop of the heavy chain as residues 26-32. This limitation is also significant because it was required for patentability.

In the Final Rejection, the Examiner argued that the limitation "outside the Kabat and Chothia CDRs" is taught, for example, on page 9, lines 1-5 of Queen '975 and page 13, lines 1-8 of Queen '252. The passages cited by the Examiner, however, do not support the Examiner's position.

The passage on page 9, lines 1-5, of Queen '975, contains a background discussion of the hypervariable regions, which it is therein stated are also called the CDRs. References by Kabat and Chothia are cited, and incorporated by reference. This is the only in

¹Notably, Chothia and Lesk, *J. Mol. Biol.*, 196:901-917, 1987, (cited at col. 15, line 43, of the Queen patent for defining CDRs) refers to hypervariable loops and carefully distinguishes these loops from the Kabat CDRs (see page 904 of the Chothia reference, attached).

DOCKET NO.: CARP-0057**PATENT**

passage in Queen '975 linking the Chothia reference to the term "CDRs." Other passages specifically referring to the CDRs as encompassed by the invention of Queen '975 make it clear that the CDRs are as defined by Kabat. For example, on page 10, line 2, the framework regions are defined in terms of Kabat. If the framework regions are defined in terms of Kabat, the CDRs must be as well. On page 21, the protocol for selecting which residues in the heavy chain are to be donor is set out. In lines 19-22, residues which fall in positions within a CDR "as defined by Kabat, [i.e.,] amino acids 31-35, 50-66, and 99-106" are to be donor. In lines 28-30, amino acid 30 is listed as a position immediately adjacent to a CDR to be changed to donor. Amino acid 30 is adjacent the heavy chain Kabat CDR, but within the heavy chain Chothia "CDR" as that term is used in Queen '975. The description of Figure 1 of Queen '975 indicates that it refers to the heavy chains and that the three CDRs are underlined (page 6, lines 1-6). In Figure 1, amino acids 31-35 are underlined for CDR1. Clearly, all specific references to CDRs in Queen '975 are to Kabat CDRs only.

The passage relied upon by the Examiner for referring to Chothia in Queen '252 is in the context of computer programs for computer models. There is no reference to CDRs. Contrastingly, the specific references to CDRs in Queen '252 make it clear that the CDRs are as defined by Kabat. On page 8, lines 22-26, Queen '252 reports that the extents of the framework region and CDRs have been "precisely defined" by Kabat. On page 21, the protocol for selecting which residues in the heavy chain are to be donor is set out. In lines 20-22, residues which fall in positions within a CDR "as defined by Kabat, [i.e.,] amino acids 31-35, 50-66, and 99-106" are to be donor. In lines 27-29, amino acid 30 is listed as a

DOCKET NO.: CARP-0057**PATENT**

position **immediately adjacent to a CDR** to be changed to donor. Amino acid 30 is adjacent the heavy chain Kabat CDR, but **within** the heavy chain Chothia "CDR" as that term is used in Queen '975. In Figure 1, amino acids 31-35 are underlined for CDR1. Clearly, all specific references to CDRs in Queen '975 are to Kabat CDRs only.

Applicants respectfully request that this rejection be withdrawn.

The Proposed Count is the same as that submitted with the Amendment filed April 9, 1999. Applicants again identify all of the Queen patent claims 1-11 and Applicants' claims 24-31 as corresponding to the Proposed Count.

In attached Appendix B, applicants illustrate the representative support in their present application disclosure for the limitations of their amended claim 24. There is, of course, additional support in applicants' application omitted for the sake of brevity.

In attached Appendix C is a diagram of support in applicants' 1989 GB application for each limitation of applicants' amended claim 28, also drawn to the same invention as proposed Count 1. Accordingly, applicants' effective filing date for their invention of Count 1 is 12/21/89, the filing date of their GB national application.

In view of the foregoing, Applicants respectfully submit that allowable subject matter has been identified and request that the Examiner declare an interference between the

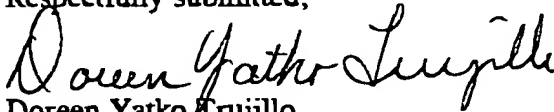
DOCKET NO.: CARP-0057**PATENT**

present application and the Queen patent.

If at least one of the presented claims is not rejectable on any [] ground and is claiming the same invention as at least one claim of the patent, the examiner should proceed to initiate an interference.

MPEP 2307.02. Applicants respectfully request that an interference between the present application and the Queen patent be declared. The Examiner is requested to contact the undersigned at (215) 564-8352 if she is of a different view.

Respectfully submitted,


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Date: May 24, 2000

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